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Prevention of cardiometabolic diseases through dietary modifications

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Abstract

Purpose of the review

Cardiometabolic diseases (CMD) increasingly contribute to the cumulative burden of morbidity and mortality worldwide. Here we reviewed intervention studies using a randomised controlled trial (RCT) design as well as meta-analyses of RCTs aimed at testing the effectiveness of different dietary approaches for CMD prevention.

Recent findings

Recent studies testing dietary approaches for CMD prevention were summarised narratively, with a focus on interventions based on caloric restriction and fasting, healthy dietary patterns and food-based dietary modifications. Evidence supports intermittent fasting, Mediterranean, Nordic, DASH, low-carbohydrate/ketogenic and plant-based diets as effective strategies for improving cardiometabolic health. However, the benefits observed with some of these dietary patterns are linked to energy restriction, and the independent effects beyond weight loss remain unclear. The effectiveness of some strategies may also depend on the overall dietary quality and adherence to the programme.

Summary

Recent findings highlight the importance of focusing on overall dietary patterns, rather than isolated nutrients, for preventing cardiometabolic disease. Future research should prioritize long-term intervention studies to assess the sustained effects of these dietary patterns on cardiometabolic disease outcomes.

Keywords

Cardiometabolic health, intermittent fasting, dietary patterns, low-carbohydrate diet, plant-based diet

Key points

- Intermittent fasting may enhance cardiometabolic health, primarily through mechanisms related to energy restriction and weight management.
- The Mediterranean, Nordic, and DASH diets, which emphasize nutrient-dense foods and balanced nutrient profiles, are strongly supported by evidence for their role in reducing cardiometabolic risk.
- Low-carbohydrate and ketogenic diets have shown efficacy in improving weight and glycaemic control, though their long-term cardiometabolic benefits remain uncertain.
- Plant-based diets have demonstrated positive effects on several cardiometabolic markers, but the overall quality of the diet is a critical factor in determining these outcomes.

Introduction

Cardiometabolic diseases (CMD), including cardiovascular diseases (CVD) and metabolic disorders such as type 2 diabetes and obesity, are leading causes of morbidity and mortality worldwide (1-3). Global estimates have reported that over 17 million people die annually from CVD (3), and the prevalence of diabetes and obesity exceeds 500 million (1, 2), with the fastest upward trends found in lower- and middle-income countries (4, 5). With the substantial economic and societal burden associated with CMD, improving cardiometabolic health is a top priority that requires greater efforts in prevention strategies, particularly those targeting critical modifiable risk factors such as suboptimal dietary habits.

Nutrition science has traditionally focused on single isolated nutrients to understand diet-related disease. A large body of evidence has investigated the role of saturated fats in dyslipidaemia or excess calorie intake on weight gain. Given the complex nature of dietary intake and the pathophysiology of CMD, focusing on dietary patterns (DP) or broader food groups may offer new insights into biological pathways leading to CMD (6). Dietary patterns, which reflect daily dietary behaviours and involve the quantities, diversity, and combination of foods and drinks habitually consumed, have become a focus of research. Some DPs, such as the Mediterranean diet and the DASH diet, have been extensively studied in association with CVD and diabetes due to their emphasis on whole foods, healthy fats, and reduced dietary sodium (7). Other interventions for reducing CMD risk have proposed strategies promoting weight loss through fasting, or changes in specific food groups, including the restriction of carbohydrate-rich foods or animal products.

This review highlights the latest evidence on the role of different dietary modifications in the prevention of CMD by examining the impact of interventions involving calorie restriction or fasting, as well as those promoting healthier DPs or controlling specific food groups. Understanding the mechanisms through which diet influences cardiometabolic health can help develop effective dietary guidelines and interventions to mitigate the global burden of CMD.

Caloric Restriction & Fasting

Traditional caloric restriction (CR) involves a calorie reduction of up to 30% of the total daily intake without manipulating any nutrient or food specifically. A network meta-analysis of RCTs implementing CR in populations with overweight/obesity and/or comorbidities, showed that CR can mostly help achieve significant reductions in body mass index (BMI) and waist circumference (8). Some evidence supports concomitant short-term CMD benefits in plasma lipids, blood pressure, glycaemic control or inflammatory biomarkers (9). The CALERIE-2 RCT implemented a 12% CR in normal-overweight individuals over 2 years and found significant improvements in traditional and emerging CMD risk markers, including a shift from lower-density to higher-density lipoproteins, reductions in branched-chain amino acids and inflammation (10). However, these effects were more pronounced in people at higher BMI levels. Considering that most of the evidence around CR has emerged from populations with overweight or obesity, more evidence is needed to understand the role of CR in CMD prevention over and above the benefits achieved through weight loss.

Fasting involves intentionally ceasing the intake of foods and drinks (other than water) over a specific period of time, without the need to monitor food intake. This approach has emerged as an alternative to CR given its simplicity to help control food intake in the longer term.

Intermittent fasting (IF) alternates periods of fasting with ad libitum eating windows that vary between hours (i.e. time restricted eating – TRE, generally 14 to 20-h of fasting/day) to days (i.e. alternative day fasting – ADF, generally alternating 24-h fast periods with unrestricted eating over the following 24-h, over several days a week) (11). ADF and TRE are widely popular IF approaches which have shown varying degrees of adherence and reductions in the total daily energy intake, hence resulting in differential effects on body weight and cardiometabolic risk (11, 12).

ADF has shown important benefits in terms of weight loss and some cardiometabolic improvements both in healthy individuals (13) and those with overweight/obesity (14-16). Some studies have shown that ADF produces larger decreases in weight loss and fat mass than TRE as well as reductions in blood lipids and blood pressure compared with *ad libitum* diets (17). For weight control in people with overweight or obesity, TRE has shown to achieve moderate weight loss (14), although it appears to be as effective as traditional CR in the long term (18). For CMD risk, evidence is generally not supporting TRE as a superior approach in the general population although there seems to be some benefits for glycaemic control and blood lipids in people with type 2 diabetes (18, 19). Some evidence supports the added benefit of aligning the eating window with the daily metabolic circadian system, with more favourable cardiometabolic improvements observed with the early TRE (20-22) although evidence from longer-term RCTs is needed to confirm this.

Compared with *ad libitum* control diets, IF approaches help achieve weight loss and improve body composition and cardiometabolic health outcomes as long as energy deficit is achieved (23, 24). When energy intakes are matched, IF provides similar benefits for weight control and CMD risk than continuous daily CR, suggesting that the energy deficit becomes the main driver of the observed benefits (24, 25). Limited and preliminary evidence suggest that IF might be beneficial in the absence of weight loss (26), which may enhance cardiometabolic health of weight stable individuals or after a weight loss intervention although this warrant further investigation.

Healthy Dietary Patterns

Mediterranean Diet

The Mediterranean diet (MD) promotes a high consumption of non-processed foods, primarily vegetables, legumes, fruits, whole grains, dairy products, oily fish and nuts as well as extra-virgin olive oil; a moderate intake of poultry, eggs, and red wine (with meals); and a low intake of red and processed meat and sweet processed foods (27). A large body of evidence has demonstrated that adherence to MD provides significant health benefits, hence numerous professional societies recommend this dietary pattern to reduce cardiometabolic risk (28).

The PREDIMED trial is one of the most influential studies which compared MD supplemented with either extra-virgin olive oil or mixed nuts along with dietary guidance, against a low-fat control diet on incident CVD. The adherence over 4.8 years of follow up to MD with either extra-virgin olive oil or mixed nuts reduced the incidence of major CVD events by about 30% (29). A higher adherence to MD over time (validated through a multi-metabolite signature) has also shown a preventative effect against type 2 diabetes (30). Similarly, the CORDIOPREV RCT has demonstrated the effectiveness of the MD over 7 years of follow up for the secondary prevention of major CVD events (31). A network meta-analysis of RCTs compared the efficacy

of MD, low-fat and low-carbohydrate dietary interventions on cardiovascular morbidity and mortality. The MD was the only dietary pattern that decreased the risk of cardiovascular death compared with control diets (32). Even in pediatric populations, the MD has been found to be superior to control or lower-fat diets for improving classical CMD risk factors such as blood pressure and lipid biomarkers (33).

Nordic Diet

The Nordic diet (ND) is grounded in the traditional Scandinavian eating habits and emphasizes the consumption of locally sourced and seasonal foods such as leafy/root vegetables, whole grains like rye and barley, berries, and fatty fish whilst reducing ultra-processed food and red/processed meat consumption (27). An expanding body of research has documented the positive impact of the Nordic DP on human health. The SYSDIET RCT, which tested an isocaloric ND on CMD risk factors in people with metabolic syndrome, has recently shown beneficial effects on glucose metabolism and blood lipids using a metabolic profiling approach (34). A meta-analysis of RCTs in people with or at risk of diabetes revealed that adherence to ND resulted in moderate improvements in key intermediate CMD biomarkers, including reductions in low density lipoprotein-cholesterol (LDL-C), high density lipoprotein -cholesterol (HDL-C), apolipoprotein B, insulin levels, body weight, BMI, and systolic blood pressure (35). Another meta-analysis of RCTs evaluating the effect of increased adherence to various dietary patterns on blood pressure reported significant reductions in systolic and diastolic blood pressure with the Nordic diet compared to control (36).

Dietary Approaches to Stop Hypertension

The Dietary Approaches to Stop Hypertension (DASH) diet, which was developed by the US National Institutes of Health in the 1990s to target hypertension, has a particular focus on dietary sodium reduction in the context of a healthy dietary pattern closely aligned with the MD. Although the DASH diet has widely demonstrated benefits for blood pressure management (37), it has also demonstrated broader effects in relation to CMD risk. A meta-analysis of RCTs of people with chronic diseases, mostly hypertension, overweight/obesity and type 2 diabetes, showed improvements with DASH diet in body weight, waist circumference and some lipids such as total cholesterol and LDL-C in addition to the expected effects on blood pressure; but no significant effects on glucose control (38, 39). However, a previous umbrella review of meta-analyses of controlled trials focusing on DASH diet and cardiometabolic risk factors found significant decreases in systolic and diastolic blood pressure, total cholesterol, LDL-C, HbA1c, fasting insulin levels and body weight. Recent data from the DASH-Sodium RCT highlighted that the prolonged adherence to this diet plays a key role in the cardioprotective effect as it led to progressive improvements in cardiovascular biomarkers and inflammation (40).

Evidence has also suggested that adherence to the DASH diet can lower blood pressure even without significant reductions in sodium intake (41). Although physiological pathways through which DASH diet exerts this effect remain elusive, evidence suggests that some of its components (i.e. higher levels of calcium and potassium from fruits and vegetables) may further contribute to the natriuretic and diuretic effects on blood pressure.

Control of specific food groups

Low-carbohydrate & Ketogenic Diets

Low-carbohydrate diets (LCDs) are based on a significant reduction of carbohydrate intake to <26% of total daily calories or <130 g/day and follow the premise that controlling insulin levels can reduce adipose tissue deposition and enhance cardiometabolic health (27). Dietary interventions based on LCDs have demonstrated effectiveness for glycaemic control and weight in people with diabetes or obesity (42, 43), and more recent studies have shown favourable changes in cardiometabolic and inflammatory markers (44-46), all of which play a significant role in CMD development. A meta-analysis of RTCs documented that, compared with lower-fat diets, LCDs reduced body weight, C-reactive protein and IL-6 levels in both overweight and healthy weight adults (47).

Ketogenic diets (KD) further restrict carbohydrate intake to ≤50 g/day whilst promoting higher fat intakes, inducing nutritional ketosis and shifting the body's energy source from glucose to ketone bodies (48). While KD have shown benefits in populations with specific CMD (49), their effectiveness in preventing these conditions in people without specific diseases is still unclear. A recent meta-analysis of RTCs in healthy individuals demonstrated positive effects of KD on triglycerides, HDL-C, blood pressure, weight loss and glycaemic control. However, KD were also associated with increases in total and LDL-C, both of which are known CVD risk factors (49). Another meta-analysis found no significant association between KD and blood pressure, suggesting that the quality of fats and protein intake may be more important than the carbohydrate-to-fat ratio (50). The inconsistency in how KD are defined across studies, particularly regarding carbohydrate content and overall macronutrient distribution (49), complicates drawing definitive conclusions. Future research must also provide detailed reporting on the quality and types of fats and proteins consumed.

Overall, carbohydrate restriction seems to help control some CMD risk factors, particularly for people with conditions such as type 2 diabetes. However, the longer-term benefits of LCDs or KD are still unclear and may rely on the quality of the diet as well as the need to ensure optimal nutrition during the dietary regime (51).

Plant-based, Vegetarian, Vegan & Low Meat Diets

Plant-based diets (PBDs) have gained popularity alongside the increasing awareness of climate change and the carbon foodprint of the diet. There is also increasing recognition that animal-based foods, particularly red and processed meats, are associated with unfavourable metabolic outcomes (52). PBDs emphasize the consumption of vegetables, fruits, whole grains, legumes, nuts, and seeds while minimizing or eliminating animal-based products. Potential benefits of PBDs on cardiometabolic risk factors include reductions in body weight and fat mass as well as improvements in lipid and inflammatory markers, blood pressure, blood glucose and insulin sensitivity, which together enhance overall metabolic health (53). The benefits of PBDs are attributed to factors such as lower energy density, higher fibre content and antioxidant levels compared to other diets, and lipid-lowering effects due to the reduced intake of saturated fats, cholesterol and total fat. However, the cardiometabolic effects of PBDs can vary based on the dietary quality. Higher-quality PBDs are associated with a reduced risk of obesity, CVD, and type 2 diabetes, whereas lower-quality PBDs, such as those based on processed meat substitutes, may not confer any cardiometabolic benefits (54, 55).

Vegan and vegetarian diets have shown potential benefits for various CMD risk factors, though the evidence is complex and sometimes inconsistent. Vegan diets eliminate all animal-derived foods while vegetarian diets exclude meat but potentially include dairy, eggs or fish depending on the type. These diets have lower energy density and are higher in fibre, vitamins, minerals and phytonutrients compared to other dietary patterns, though they may limit specific nutrients (e.g., vitamin B12, iron, calcium). One RCT comparing vegan vs. omnivorous diets in healthy identical twins found that the vegan diet led significantly lower LDL-C, insulin levels, and body weight (56). Interestingly, trimethylamine N-oxide (TMAO) levels, a potential CVD risk marker, did not differ significantly between the two diets, despite prior studies suggesting lower TMAO levels in vegans due to reduced intake of animal-derived choline and carnitine (56). A meta-analysis of RCTs focusing on key atherogenic lipids and lipoproteins reported significantly lower levels of total cholesterol, LDL-C and apolipoprotein B with vegetarian and vegan diets; though found smaller reductions in total cholesterol in people with obesity than normal or overweight status, potentially due to the negative impact of obesity on cholesterol metabolism (55). Evidence from a meta-analysis of RCTs indicates that adherence to vegan and vegetarian diets can improve insulin sensitivity in the short-term, as evidenced by reductions in HOMA-IR and fasting insulin levels in individuals with overweight or obesity (53). Further evidence from longer-term RCTs is necessary to establish the potential benefits for people at risk of or with type 2 diabetes.

Plant-based, vegetarian or vegan diets generally show benefits for CMD prevention. It remains uncertain whether the observed benefits of PBDs are driven by the dietary composition or are confounded by factors like weight loss, which typically improves CMD risk factors. It is also not clear whether the effects of modern plant-based, which more closely resemble current eating habits based on lower quality processed foods, align with those observed in traditional plant-based diets (57).

Evidence regarding the cardiometabolic effects of diets with reduced red and processed meat intakes is progressively growing albeit largely observational. Whilst cohort studies have suggested a potential association between overall red meat intake and increased CMD risk (52), RCTs have not consistently supported a definitive link and most trials have evaluated short-term changes in biomarkers, rather than long-term disease outcomes (58). Additionally, inconsistencies regarding the cardiometabolic benefits of reducing red meat consumption may be partly explained by the comparison diet. A meta-analysis of RCTs that replaced red meat with a variety of foods reported that only the replacement with high quality plant protein, as opposed to fish or other carbohydrates, resulted in more favourable changes in CVD risk factors (59). Other meta-analyses of RCTs investigating the effect of reduced red meat intake showed no significant impact on biomarkers related to type 2 diabetes risk or inflammation in adults with CMD risk (58, 60). The impact of eating unprocessed red meat on CMD remains largely inconclusive, with no clear beneficial or detrimental effects identified.

Future research directions

Future studies on caloric restriction and intermittent fasting should focus on populations beyond those with excess weight to better understand their specific role on CMD prevention, independent of weight loss. Longer-term RCTs testing if time-restricted eating is effective in the absence of weight loss for improved cardiometabolic health are needed, particularly when meals are consumed earlier in the day. For the DASH dietary approach, the underlying

physiological mechanisms by which this diet can lower blood pressure even without sodium reduction needs further exploration. Research on low-carbohydrate and ketogenic diets shows beneficial effects in people with type 2 diabetes, yet the long-term health impacts need a better evidence base, emphasizing the importance of diet quality and adherence to the programme. Plant-based diets generally show benefits for CMD prevention, though it remains unclear whether the effects are related to the dietary composition or related to weight loss. Additionally, while reduced red and processed meat intake shows potential CMD benefits, long-term intervention studies focused on disease outcomes rather than intermediate risk factors are needed, as well as further research on the effects of unprocessed red meat on CMD risk.

Conclusion

Several dietary strategies have been proposed to mitigate cardiometabolic risk; however, the long-term benefits for many of these approaches remain unclear. Traditional caloric restriction has primarily demonstrated effectiveness for weight management, with some evidence suggesting improvements in CMD markers. Intermittent fasting has gained popularity in recent years, yet evidence suggests that its cardiometabolic benefits are most pronounced when an overall energy deficit and weight loss are achieved. Dietary patterns such as the Mediterranean, Nordic, and DASH diets are well-supported by the scientific evidence for their cardiometabolic improvements. These dietary approaches are closely aligned and emphasize the consumption of traditional, locally sourced nutrient-dense foods while limiting processed foods high in sodium, added sugars, and saturated fats. Low-carbohydrate and ketogenic diets have shown promise, particularly among individuals with metabolic conditions such as type 2 diabetes. Plant-based diets that emphasise high-quality, minimally processed foods have broadly demonstrated CMD benefits. Indeed, substituting red and processed meats with high-quality plant-based protein appears to be an effective strategy for managing cardiometabolic disease.

In practice, these different dietary strategies can often work synergistically to optimize metabolic health. A balanced intake of nutrients, the inclusion of high-quality food sources, and the identification of strategies that promote long-term adherence may play a critical role in the prevention and management of cardiometabolic disease.

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Conflicts of interest
There are no conflicts of interest.

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